

Survival and Functionality of hESC-Derived Retinal Pigment Epithelium Cells Cultured as a Monolayer on Polymer Substrates Transplanted in RCS Rats.

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Authors: Biju B Thomas, Danhong Zhu, Li Zhang, Padmaja B Thomas, Yuntao Hu, Hossein Nazari, Francisco Stefanini, Paulo Falabella, Dennis O Clegg, David R Hinton, Mark S Humayun

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Public Summary:

These results demonstrate the safety, survival, and functionality of the hESC-RPE (human embryonic stem cells) monolayer transplantation in an RPE dysfunction rat model.

Scientific Abstract:

PURPOSE: To determine the safety, survival, and functionality of human embryonic stem cell-derived RPE (hESC-RPE) cells seeded on a polymeric substrate (rCPCB-RPE1 implant) and implanted into the subretinal (SR) space of Royal College of Surgeons (RCS) rats. **METHODS:** Monolayers of hESC-RPE cells cultured on parylene membrane were transplanted into the SR space of 4-week-old RCS rats. Group 1 (n = 46) received vitronectin-coated parylene membrane without cells (rMSPM+VN), group 2 (n = 59) received rCPCB-RPE1 implants, and group 3 (n = 13) served as the control group. Animals that are selected based on optical coherence tomography screening were subjected to visual function assays using optokinetic (OKN) testing and superior colliculus (SC) electrophysiology. At approximately 25 weeks of age (21 weeks after surgery), the eyes were examined histologically for cell survival, phagocytosis, and local toxicity. **RESULTS:** Eighty-seven percent of the rCPCB-RPE1-implanted animals showed hESC-RPE survivability. Significant numbers of outer nuclear layer cells were rescued in both group 1 (rMSPM+VN) and group 2 (rCPCB-RPE1) animals. A significantly higher ratio of rod photoreceptor cells to cone photoreceptor cells was found in the rCPCB-RPE1-implanted group. Animals with rCPCB-RPE1 implant showed hESC-RPE cells containing rhodopsin-positive particles in immunohistochemistry, suggesting phagocytic function. Superior colliculus mapping data demonstrated that a significantly higher number of SC sites responded to light stimulus at a lower luminance threshold level in the rCPCB-RPE1-implanted group. Optokinetic data suggested both implantation groups showed improved visual acuity. **CONCLUSIONS:** These results demonstrate the safety, survival, and functionality of the hESC-RPE monolayer transplantation in an RPE dysfunction rat model.

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